REMARKS

Claim Amendments

Responsive to the Examiner's request in item 1 of the Office Action, Applicants are cancelling herewith withdrawn claims 43 and 45-54, without prejudice or disclaimer.

Dependent claims 56 and 66 are cancelled herein without prejudice or disclaimer, and without effecting the scope of the independent claims, for reasons unrelated to patentability.

Section 102

The Examiner maintains the Section 102(e) rejection on the basis that the disclosure of Hudziak et al. "teaches the use of vinca drugs in combination with an anti-ErbB2 antibody" and because "vinorelbine is also a vinca drug and because not all possible drugs within a class of drugs could be listed, the claimed invention is still anticipated."

Applicants submit that the presently claimed invention is not anticipated by Hudziak et al.

First, Applicants respectfully submit that the rejection appears to be premised on an incorrect characterization of the disclosure of the cited reference. In particular, Hudziak et al. refer to the "vinblastine" species (column 6, line 64) rather than the vinca "class of drugs" as suggested by the Examiner. Since the rejection seemingly requires that the art teach the *class* of vinca drugs, Applicants respectfully submit that, since Hudziak et al. only disloses the Vinblastine *species*, the rejection should fall given that even assuming arguendo the Office had shown disclosure of the genus (vinca drugs in general) anticipates the species (Vinorelbine) - which is denied, see below - the Office has nowhere shown how the (Vinblastine) species anticipates another distinct species

(Vinorelbine)[1].

Second, Applicants submit that the Office not proven anticipation. See MPEP 2131.

> "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. V. Union Oil Co. of California*, 814 F. 2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). "The identical invention must be shown in as complete detail as is contained in the ... claim." *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989).

Applicants submit that the claims are not anticipated because the art does not teach, either expressly or inherently, "each and every element" as set forth therein, namely, the Office has not shown where the reference describes the *Vinorelbine* element of the claims. Disclosure of the Vinblastine species (in Hudziak et al.) does not teach, expressly or inherently, Vinorelbine (as claimed herein). The identical invention is not shown in as complete detail in Hudziak et al. as is contained in the present claims.

To the extent the Office urges that Vinorelbine and Vinblastine are the same, even inherently, Applicants submit that the ordinarily skilled clinician would readily appreciate this is simply not the case. This is illustrated by reference to the attached internet excerpt entitled "*Parmacology of Vinblastine, Vincristine, Vindesine and Vinorelbine*" which notes that Vinorelbine is structurally and

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[1]Applicants believe the rejection may have been carried over from an earlier rejection where the pending claim recited the "vinca" genus, but note that the claims have now been amended to recite the "Vinorelbine" species instead. That particular species, Vinorelbine, is not described in Hudziak et al.

functionally distinct from Vinblastine, for instance having a wider range of antitumor activity than Vinblastine. Hence, it is clear that Vinorelbine (in present claims) and Vinblastine (in cited art) are simply not the same compound.

Finally, Applicants note that the Office has previously taken the position that different chemotherapeutic products (here Vinblastine or Vinorelbine) are "completely different products, having different structures, and different pharmaceutical effects" (Office Action dated 2/15/2002, page 5, under item B), and therefore claims to different chemotherapeutic agents are "patentably distinct." Hence, Applicants submit that the presently claimed combination with Vinorelbine is, according to the Office, patentably distinct from the combination with Vinblastine in Hudziak et al. The Office has not even shown that Vinorelbine was known in 1988, the effective filing date of Hudziak et al.

Hence, for any one or more of the reasons elaborated above, Applicants submit that the invention set forth in claims 42, 44 and 63 is not anticipated by Hudziak et al. and reconsideration and withdrawal of the Section 102(e) rejection is respectfully requested.

Obviousness-type Double Patenting

Claims 42, 44, 55, 63 and 65 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 4, 22 and 23 (Applicants assume claim 33 is intended) of US Patent No. 5,720,954.

In order to expedite prosecution, and without acquiescing in the rejection, Applicants submit herewith a terminal disclaimer over the '954 patent. Reconsideration and withdrawal of the rejection is respectfully requested in view of the terminal disclaimer submitted herewith.

Serial No. 09/705,579

Related Case Statement

Applicants submit herewith a Related Case Statement, and ask the Examiner to consider the related applications with respect to the prosecution of the present application.

Applicants believe that this application is in condition for allowance, and look forward to early receipt of same.

Respectfully submitted,
GENENTECH, INC.

Date: March 1, 2004

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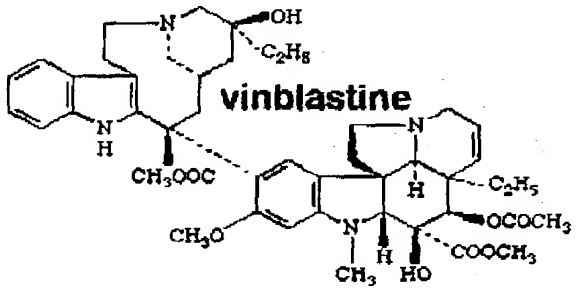
Pharmacology of Vinblastine, Vincristine, Vindesine and Vinorelbine

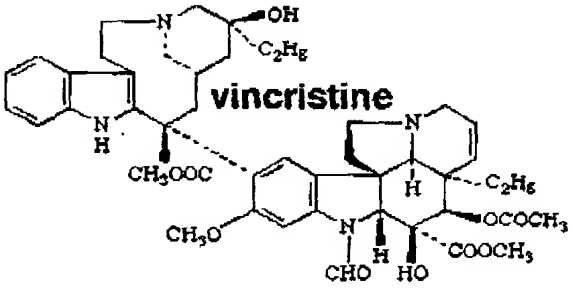
[Chemical Comparison Table | Periwinkle Page]

Vinblastine and **vincristine** are alkaloids found in the Madagascar periwinkle, *Catharanthus roseus* (formerly classified as *Vinca rosea*, which led to these compounds becoming called **Vinca alkaloids**).

They and **vindesine** and **vinorelbine**, semisynthetic derivatives of vinblastine, all work by inhibiting **mitosis** (cell division) in **metaphase**. These alkaloids bind to **tubulin**, thus preventing the cell from making the **spindles** it needs to be able to move its chromosomes around as it divides (this is similar to the action of colchicine, but is different fr om the action of paclitaxel, which interferes with cell division by keeping the spindles from being broken down). These alkaloids also seem to interfere with cells' ability to synthesize **DNA** and **RNA**. They are all administered intravenously in their sulfate form once a week; these solutions are fatal if they're administered any other way, and can cause a lot of tissue irritation if they leak out of the vein. Although these three compounds are very similar in structure and have the same basic action, they have distinctly different effects on the body.



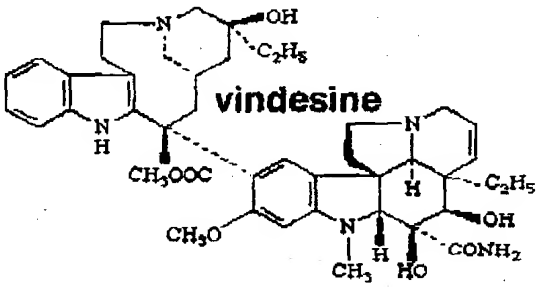
Vinblastine is typically administered at a dose of 6 milligrams per square meter of body surface. It's marketed as Velban by Eli Lilly and has a half-life in the bloodstream of 24 hours. Vinblastine is mainly useful for treating Hodgkin's disease, lymphocytic lymphoma, histiocytic lymphoma, advanced testicular cancer, advanced breast cancer, Kaposi's sarcoma, and Letterer-Siwe disease. It also seems to fight cancer by interfering with glutamic acid metabolism (specifically, the pathways leading from glutamic acid to the Krebs cycle and to urea formation). People with bacterial infections should not be given this drug, nor should pregnant women, since it caused severe birth defects in animal studies. Side effects include hair loss, nausea, lowered blood cell counts, headache, stomach pain, numbness, constipation and mouth sores. Bone marrow damage is the typical dose-limiting factor.



Vincristine, which is marketed as Oncovin by Eli Lilly, has a serum half-life of about 85 hours. It's used mainly to treat acute leukemia, rhabdomyosarcoma, neuroblastoma, Hodgkin's disease and other lymphomas. The typical dose in 1.4 milligrams per square meter of body surface once a week, and neurotoxicity is the dose limiting factor (it can cause damage to the peripheral nervous system). Because of this, people with neuromuscular disorders should steer clear of this drug if possible. Likewise, people with some forms of Charcot-Marie-Tooth syndrome should

avoid vincristine. Pregnant women should definitely not take it, because it causes severe birth defects in animal tests. Side effects include those found with vinblastine, plus nervous system problems such as sensory impairment; some people may also develop breathing problems or lung spasms shortly after the drug is administered. People occasionally develop secondary cancers if they receive the drug along with other anticancer drugs that are known to be carcinogens.

Vindesine has a serum half-life of about 24 hours and is administered at a dose of 3 milligrams per square meter of body surface. Its toxicity and side effects are similar to those of vinblastine. Vindesine, which is marketed under the names Eldisine and Fildesin, is used mainly to treat melanoma and lung cancers (carcinomas) and, with other drugs, to treat uterine cancers.



Vinorelbine is currently in Phase II clinical trials as a treatment for ovarian cancer. It will be marketed as Navelbine by Glaxo Wellcome, Inc., if the trials are successful and the FDA approves the drug. Thus far, vinorelbine seems to have a wider range of antitumor activity than the other vinca alkaloids. In preclinical trials, it showed promise in treating patients with epithelial ovarian cancers and, in combination with the chemotherapy drug cisplatin, in treating patients with non-small-cell lung cancers. The side effects of this drug include diarrhea, nausea, and hair loss; it seems to be less of a nerve poison than vindesine.

For more information, visit:

- Ovarian Cancer Research Notebook: Vinorelbine (Navelbine)
- Vincristine Fact Sheet From the National Cancer Institute
- The Access Project: Vinblastine
- The Access Project: Vincristine
- Understanding Vindesine: Uses and Side Effects

References:

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